Multiple Discordant Histology After Nephrectomy: Descriptive Analysis and Outcomes

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Abstract

Renal-cell carcinoma (RCC) is the most common primary renal neoplasm, but few cases of ipsilateral renal lesions of different RCC histologic subtypes have been described. We present a novel finding of 2 distinct histologic patterns present within the same tumor in addition to the largest cohort of synchronous renal tumors, of which clear-cell with chromophobe RCC was the most common pairing.

Background: While RCC is the most common primary renal neoplasm, few cases of ipsilateral renal lesions of different RCC histologic subtypes have been described. The objective of this study was to evaluate our experience with synchronous, histologically unique, primary renal neoplasms within the same kidney. **Patients and Methods:** We retrospectively analyzed 2 institutional nephrectomy databases from 2000 to 2013. The study cohort comprised 15 patients with multiple, discordant renal histology after partial or radical nephrectomy. Demographic data, immunohistochemical analysis, and clinical course were assessed and analyzed. **Results:** Eight patients (53%) were black, 10 (60%) were male, and 5 (36%) were tobacco users. Median follow-up time was 13 months (range, 1-62 months), and 9 patients (56%) underwent radical nephrectomy. Among 36 tumors, the median tumor size was 2.3 cm (range, 0.4-9 cm). The most common combination of discordant tumor histology among patients with $\geq$ 2 tumors was clear-cell (cc) renal-cell carcinoma (RCC) with chromophobe RCC (3 cases, 19%). In 3 patients (19%), a single tumor was noted to have 2 distinct patterns; all patients had ccRCC with papillary RCC. Three (20%) of 15 patients developed metastatic disease. The median cancer-free survival time for patients with metastasis was 2 months. **Conclusion:** Multiple, discordant renal pathology represents a rarely reported entity in patients receiving nephrectomy. We introduce the largest cohort of synchronous renal tumors, of which ccRCC/chromophobe RCC was the most common pairing.

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Introduction

Renal-cell carcinoma (RCC) arises from the epithelium of the renal tubules and accounts for nearly 80% of all primary renal neoplasms. In 2014 there were a predicted 63,920 new cases of kidney and renal pelvis cancer diagnoses and approximately 13,860 deaths.[1] Male subjects are affected twice as frequently as female subjects, with a peak incidence in the sixth or seventh decade of life.[2] Of the histologic subtypes, the 3 most common include clear-cell (cc) RCC, accounting for 75% of RCC cases, followed by papillary RCC (pRCC), 10% of cases, and chromophobe RCC, 5% of cases.[2,3] An emerging subtype of clear-cell papillary RCC (cc-pRCC) has recently been reported in the literature. This class of RCC has both clear-cell and papillary features on histology; however, it displays unique genetic and histologic features.[4]

While RCC is the most common primary renal neoplasm, few cases of ipsilateral renal lesions of different RCC histologic subtypes have been described. Capaccio et al[5] identified 5 cases in patients with 2 distinct tumors in the same kidney bearing different histology. Four other case reports have described variations of ccRCC with other histologic patterns.[6-9]

The objective of the current study was to describe what is to our knowledge the first case of 2 distinct histologic subtypes of RCC presenting within a single tumor. We also describe the largest

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experience of multiple ipsilateral RCC of different histology, including clinicopathologic variables, treatment, and long-term outcomes.

Materials and Methods

Study Population

After obtaining institutional review board approval at both institutions, we constructed a comprehensive retrospective database of all patients from Georgia Regents University and Emory University who underwent radical or partial nephrectomy from January 2000 to April 2013 (Georgia Regents University, n = 510; Emory University, n = 2307; total, n = 2817). All patients with multiple discordant renal histology were identified and included in the analysis (n = 15, 0.53%). Demographic data were reviewed, including age, gender, ethnicity, smoking history, Charlson comorbidity index, and body mass index. Surgical data included whether the procedure was a radical or partial nephrectomy and the surgical approach (open vs. laparoscopic vs. robot-assisted laparoscopic). Cancer-specific data included tumor laterality, number of tumors per kidney, mean tumor size, tumor histology, and recurrence. Time to follow-up was calculated from the date of surgery to the most recent clinic visit or the censoring date. Overall survival and time to metastasis were calculated for each individual patient.

Pathologic Evaluation

All partial or radical nephrectomies specimens were reviewed by genitourinary surgical pathologists. Specimens were inked on the outer surface after submission of vascular and ureteral margins. The kidney specimen was then bivalved to identify the tumor or tumors and their relation to other anatomic structures, including renal pelvis, renal vein, perinephric fat, hilar fat, and adrenal gland, if present. Measurements were taken including tumor size and distance from the nearest anatomic structures. Sections of the tumor, with attention to the relation to other structures, were then submitted for microscopic examination. Special stains included, but were not limited to, CK7, CD10, vimentin, CD117, α-methylacyl coenzyme A racemase (AMACR), E-cadherin, and Hale colloidal iron. These stains are used in tumors that are difficult to classify histologically or to confirm multiple ipsilateral tumors in select cases that may appear similar histologically.

Results

Table 1 summarizes the demographic and clinical data for the identified patients. There were 15 patients with multiple, discordant renal histology. One of the 15 patients had bilateral discordant renal pathology, for a total of 16 cases. The median age was 64 years (range, 44-89 years). Five patients (33%) were female. Eight patients (53%) were black, 5 (33%) were white, 1 (7%) was Asian, and 1 (7%) was Hispanic. The median Charlson comorbidity index was 6 (range, 1-8). Of the 15 patients, 5 (33%) were current or former smokers. The median time to follow-up was 13 months (range, 1-62 months). Of the 16 procedures performed, 9 (56%) were radical and 7 (44%) were partial nephrectomies. There were 11 open (69%), 4 laparoscopic (25%), and 1 robotic (6%) procedure.

Table 2 summarizes the operative and histologic outcomes. A total of 36 tumors were identified at pathology. Tumor size ranged from 0.4 to 9.0 cm, with a median size of 2.3 cm. Thirteen of the 16 cases were patients with ≥ 2 tumors in a single kidney. Of these 13 cases, the most common discordant tumor histology combination was ccRCC with chromophobe RCC (19%, 3 cases). The remaining histology pairings were pRCC with cc-pRCC (13%, 2 cases), ccRCC with cc-pRCC (13%, 2 cases), ccRCC with pRCC (13%, 2 cases), and pRCC with acquired cystic-disease RCC (13%, 2 cases). In 3 patients (19%), a single tumor was noted to have 2 distinct patterns. All 3 patients had ccRCC with pRCC (Figure 1), with 1 of the patients having > 5% sarcomatoid features. There were no discordant RCC + oncocytoma pairings in our series.

Table 1 Demographic and Clinical Data

Patient No.	Age (Years)	Gender	Ethnicity	CCI	Tobacco	BMI (kg/m^2)
1	56	M	Hispanic	3	N	28.7
2	78	F	Black	8	N	28.4
3	66	M	Black	6	N	21.6
4	74	F	White	5	Y	33.3
5	43	M	Black	3	Y	30.4
6	63	F	Black	7	N	37.9
7	50	F	White	4	Unknown	25.3
8	88	F	Asian	5	N	19.4
9	75	M	Black	5	Y	23.9
10	62	M	Black	6	Y	24.4
11	64	M	Black	5	N	33.8
12	74	M	White	6	N	25.4
13	56	F	White	1	Y	25.9
14	60	M	Black	6	N	28.3
15	75	M	White	7	N	24.8
Median	64			6		26.92

Abbreviations: BMI = body mass index; CCI = Charlson comorbidity index.

Three (20%) of 15 patients developed metastatic disease. Two of the 3 patients with metastasis were noted to have a single tumor with ccRCC and pRCC, as confirmed by immunohistochemical staining with CK7 (Figure 2A), CD10, vimentin, and AMACR (Figure 2B). The remaining patient with metastasis had pRCC with an unclassified RCC. The median disease-free survival time for patients with metastasis was 2 months.

Discussion

Although RCC accounts for the majority of primary renal neoplasms, the presence of discordant RCC pathology is a rarely reported entity. The current study represents what is to our knowledge the first multi-institutional study, and the largest to date, to investigate synchronous discordant pathology for RCC. We found that the most common discordant RCC pathology pairing was ccRCC/chromophobe RCC; we reported 3 patients with a single tumor having 2 distinct histologic patterns.

A review of the literature reveals several case reports, but only 1 case series, regarding synchronous discordant RCC.[5-9] In 2009, Capaccio et al[5] reported computed tomographic (CT) findings of 5 patients with synchronous parenchymal renal tumors of different histology in the same kidney. The 5 cases included 3 patients with ccRCC with pRCC, 1 case of ccRCC with chromophobe RCC, and